The Structures of Three New Meliacins Isolated from *Khaya anthotheca* Heartwood

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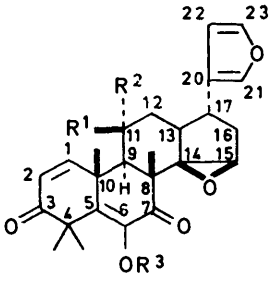
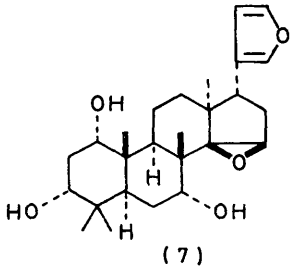
Further examination of the light petroleum extract of the heartwood of *Khaya anthotheca* has led to the isolation of 24-methylenecycloartanol, a new compound $C_{30}H_{52}O$, azadirone (9), and three new meliacins in addition to the already reported anthothecol (1). The new meliacins have been shown to be 11β-acetoxyazadirone (10), 11α-acetoxyazadirone (11), and 1α,11:14β,15β-diepoxy-6-hydroxymeliaca-5,9,20,22-tetraene-3,7-dione (20) with a novel dihydrofuran ring. The ^{13}C n.m.r. spectra of compound (20) and of related meliacins have been analysed.

THE *Khaya* genus (Meliaceae) consists of six species native to Africa. Two of these, *K. ivorensis* and *K. anthotheca*, are the principal sources of african mahogany. They are found in the high forests of West Africa, although an eastern form of *K. anthotheca* is known. The meliacin chemistry of the genus has been surveyed by Taylor and Styles and their co-workers,[1] who outlined a chemical means of distinguishing between heartwoods of the species and also pointed out that the western and eastern forms of *K. anthotheca* were different chemically. The western variety was unique in the genus because it gave no ring-D-expanded meliacins, in contrast to the other species.

Previous investigations into the timber of the western form of *K. anthotheca* have only shown the presence of anthothecol (1) and its 11-deacetyl derivative (2).[2,3] Investigations[4] of the root, root bark, and seeds of this species have shown the presence respectively of anthothecol, anthothecol and cedrelone (3), and derivatives of



(1) $R^1 = H, R^2 = OAc, R^3 = H$
(2) $R^1 = H, R^2 = OH, R^3 = H$
(3) $R^1 = H, R^2 = H, R^3 = H$
(4) $R^1R^2 = O, R^3 = H$
(5) $R^1 = H, R^2 = H, R^3 = Ac$
(6) 1,2-Dihydro-(1)



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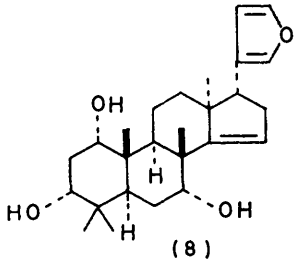

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havanensin (7) and deoxyhavanensin (8). In connection with the isolation of a number of meliacins for other studies we have had occasion to extract a commercial sample of the wood of *K. anthotheca*. A t.l.c. examination of the crude petroleum extract showed the presence of a complex mixture of meliacins and these have been investigated further.

The crude extract was obtained as a gum in 0.48% yield. A small amount of β-sitosterol was obtained from it by crystallisation from ether–methanol, but the bulk of the extract was chromatographed on deactivated alumina. Gradient elution with ether–light petroleum afforded a number of crude fractions, some of which were investigated by preparative layer chromatography (p.l.c.). Not all the crude fractions were investigated in detail because of lack of material but t.l.c. showed the presence of further meliacins which are not dealt with in this paper.

From the fractions which were investigated seven compounds, including five meliacins, were obtained. One was 24-methylenecycloartanol. The second non-meliacin (compound A) was isolated in very small amounts. Mass spectrometry indicated a formula $C_{30}H_{52}O$ but spectroscopic data did not permit assignment of a definitive structure. Because of lack of material the compound has not been investigated further.

Of the five meliacins two were the known compounds anthothecol (1) and azadirone (9).[5,6] The other three compounds, B—D, were new and have been shown to be 11β-acetoxyazadirone (10), 11α-acetoxyazadirone (11), and the enol ether (20) (1α,11:14β,15β-diepoxy-6-hydroxymeliaca-5,9,20,22-tetraene-3,7-dione).

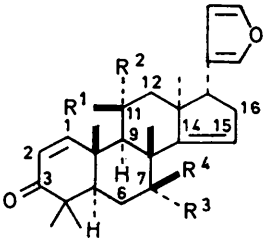
Compound B, $C_{30}H_{38}O_6$, was obtained in 0.004% yield. Its i.r. and n.m.r. spectra indicated it to be a tetranortriterpene diacetate. Except for the methyl region its n.m.r. spectrum was very similar to that of azadirone (9) apart from the presence of a second acetate peak and a broad one-proton multiplet at τ 4.25 due to the proton geminal to the acetoxy-group. The possible positions for an additional acetoxy-group in the azadirone ring system are C-6, C-11, C-12, and C-16. Only C-11 accounts for the multiplicity of the signal at τ 4.25. The other positions would give rise to quartets. This evidence indicated that compound B was an 11-acetoxyazadirone. Mild hydrolysis of compound B gave a

[1] G. A. Adesida, E. K. Adesogan, D. A. Okorie, D. A. H. Taylor, and B. T. Styles, *Phytochemistry*, 1971, **10**, 1845.
[2] C. W. L. Bevan, J. W. Powell, and D. A. H. Taylor, *J. Chem. Soc.*, 1963, 980.
[3] C. W. L. Bevan, A. H. Rees, and D. A. H. Taylor, *J. Chem. Soc.*, 1963, 983.
[4] E. K. Adesogan, D. A. Okorie, and D. A. H. Taylor, *J. Chem. Soc.* (*C*), 1970, 205.
[5] D. Lavie, E. C. Levy, and M. K. Jain, *Tetrahedron*, 1971, **27**, 3927.
[6] J. G. St. C. Buchanan and T. G. Halsall, *Chem. Comm.*, 1969, 1493.

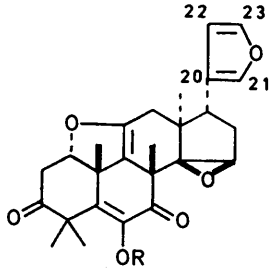
monoacetate (12), which under more vigorous conditions gave the diol (13). The hindered nature of 7α-substituents in the apotirucallane series is already known. The C-11 proton in the diol (13) gave rise to a multiplet at τ 5.26. Oxidation of the diol with chromium trioxide–pyridine complex in dichloromethane gave a hydroxy-diketone (14) as a gum which was oxidised further to the triketone (15). In the n.m.r. spectra of the diketone (14) and the triketone (15) the C-9 proton signal appeared as a singlet at τ 6.90.

Compound C was obtained in 0.003% yield. It was isomeric with compound B and their mass spectra were almost identical. Its n.m.r. spectra again resembled that of azadirone but with an additional acetate signal and a broad one-proton multiplet at τ 4.66. The methyl region was different from those of azadirone and compound B. This evidence indicated that compound C was the C-11 epimer of compound B. This conclusion was confirmed by hydrolysis of compound C to a diol (16) which was oxidised to the hydroxy-diketone (14) and thence to the triketone (15) already obtained starting from compound B.

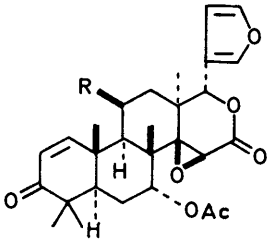
Application of the Karplus equation to determine which was the 11α-acetoxyazadirone and which the 11β-derivative was impossible since with both compounds the C-11 protons gave broad multiplets which were poorly resolved and of similar bandwidth. An assignment could be made, however, from a consideration of the chemical shifts of the angular methyl groups in compounds B and C and in azadirone. Examination of models indicates that in the 11α-acetoxy-derivative the shift of the methyl group at C-10 should be affected to a moderate extent whereas in the 11β-isomer the shifts of the methyl groups at C-8 and C-10 should be strongly influenced by the acetate function.



(9) R^1 = H, R^2 = H, R^3 = OAc, R^4 = H
(10) R^1 = OAc, R^2 = H, R^3 = OAc, R^4 = H
(11) R^1 = H, R^2 = OAc, R^3 = OAc, R^4 = H
(12) R^1 = OH, R^2 = H, R^3 = OAc, R^4 = H
(13) R^1 = OH, R^2 = H, R^3 = OH, R^4 = H
(14) R^1R^2 = O, R^3 = OH, R^4 = H
(15) R^1R^2 = O, R^3R^4 = O
(16) R^1 = H, R^2 = OH, R^3 = OH, R^4 = H
(17) 1,2-Dihydro-(9)
(18) 1,2-Dihydro-16-Oxo-(9)
(19) 16-Oxo-(9)



(20) R = H
(21) R = Me
(22) 20,21,22,23-Tetrahydro-(20)



(23) R = H
(24) R = OAc

TABLE 1

Chemical shifts (τ) of methyl n.m.r. signals *

Compound	Methyl groups at C-4	C-8	C-10	C-13
Compound B (10)	8.92, 8.92	8.50	8.55	9.23
Compound C (11)	8.91, 8.93	8.71	8.73	9.14
Azadirone (9)	8.90, 8.90	8.77	8.80	9.19
Azadiradione (19)	8.92, 8.92	8.65	8.73	8.97
Dihydroazadirone (17)	8.93, 8.95	8.80	8.90	9.20
Dihydroazadiradione (18)	8.97, 8.97	8.70	8.90	8.98
Gedunin (23)	8.93, 8.93	8.85	8.75	8.78
11β-Acetoxygedunin (24)	8.89, 8.89	8.67	8.59	8.80

* Solutions in $CDCl_3$.

The methyl signals in azadirone have been assigned (see Table 1) by comparison of the n.m.r. spectra of azadirone (9),[6] azadiradione (19),[5] dihydroazadirone (17),[7] and dihydroazadiradione (18).[5] Comparison of the signals of compounds B and C with those of azadirone indicate that compound B is the 11β-isomer and compound C the 11α-isomer. This conclusion is further supported by a comparison with the methyl shifts of gedunin (23) [8] and 11β-acetoxygedunin (24).[9]

Compound D, $C_{26}H_{28}O_6$, (20) was obtained crystalline in 0.004% yield. Its n.m.r. spectrum showed three furan protons typical of a meliacin and five methyl singlets, one of which had an unusually high chemical shift of τ 9.57, but no signals due to a Δ^1-3-one system. A diosphenol group was indicated by an absorption

[7] J. G. St. C. Buchanan and T. G. Halsall, *J. Chem. Soc.* (*C*), 1970, 2280.

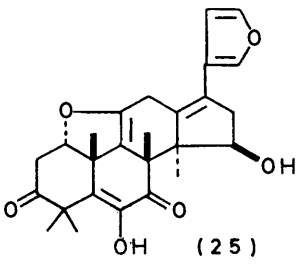
[8] M. Welford, D.Phil. Thesis, Oxford, 1964.

[9] J. D. Connolly, R. McCrindle, K. H. Overton, and J. Feeny, *Tetrahedron*, 1966, **22**, 891.

band at 276 nm (ε 10 000) which shifted to 331 nm (ε 6 000) on addition of alkali. The hydroxy-group of this system gave rise to a narrow i.r. band at 3 415 cm^{-1} and to a sharp n.m.r. singlet at τ 3.46. These figures agree with those [2,10–12] for the diosphenol system of cedrelone (3) [$\lambda_{max.}$ 279 (ε 9 100) and 327 nm (5 600); $\nu_{max.}$ 3 415 cm^{-1}; τ 3.45] and anthothecol (1) [$\lambda_{max.}$ 281 (ε 11 000) and 326 nm (4 600); $\nu_{max.}$ 3 425 cm^{-1}; τ 3.51]. Compound D is therefore a meliacin with a diosphenol group in ring B. Methylation of compound D with methyl iodide under basic conditions [2] gave the methyl ether (21). Its n.m.r. spectrum indicated that no other change had occurred during methylation.

Compound D gave a signal at τ 6.05 which is assigned to the C-15 proton of a 14,15-epoxide system of the type found in cedrelone (signal at τ 6.23) and anthothecol (τ 6.22). Treatment of compound B with sulphuric acid under anhydrous conditions gave a non-crystallisable product identified as the iso-derivative (25) analogous to isocedrolone (26) and isoanthothecol (27) previously obtained [3,10] from the natural meliacins by treatment with boron trifluoride–ether complex. A sample of isoanthothecol was prepared for comparison by treating anthothecol with sulphuric acid. All three iso-compounds absorb in the 230—240 nm region (vinylfuran chromophore).

These results showed that compound D contained the same ring B and D systems as anthothecol. Two oxygen atoms still remained to be assigned. One is a ketonic oxygen ($\nu_{max.}$ 1 720 cm^{-1}) and is placed at C-3 on the basis of arguments presented later. The i.r. spectrum of compound D also showed a band at 1 668 cm^{-1} of high intensity which was tentatively assigned to an olefinic double bond. Consideration of the evidence so far given and of the number of hydrogen atoms indicated the presence of three further rings or double-bond equivalents. It appeared likely that rings A and C of a meliacin were intact as in partial structure (28) leaving one additional ring or double bond and one oxygen atom to be accounted for.



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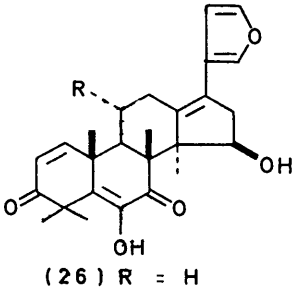
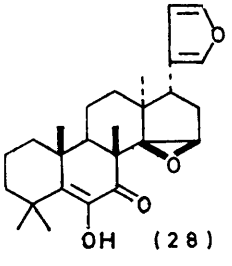
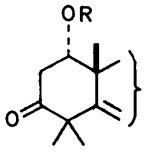


(26) R = H
(27) R = OAc



(28)



(29) R ≠ H

The only remaining low-field signals in the n.m.r. spectrum to be assigned were a coupled one-proton triplet at τ 5.47 and a two-proton doublet at τ 7.08. When either signal was irradiated the other collapsed to a singlet. These signals could be assigned to the C-1 and C-2 protons, respectively, in partial structure (29) with an oxygen function at C-1. The absence of any signal due to an olefinic proton showed that the olefinic double bond indicated by the i.r. band at 1 668 cm^{-1} must be tetrasubstituted. The position of the signal due to the proton at C-1 is not consistent with a simple hydroxy-function. It would agree with an ester or lactonic function at C-1 but this is excluded by the absence of an ester or lactonic carbonyl oxygen. Structure (20) however fits the facts. It accounts for the C-1 proton signal since the C-1 oxygen is also attached to trigonal carbon and it also accounts for the additional ring. The enol ether structure also explains the intensity and position of the olefinic i.r. band. Examination of models suggests that the oxygen at C-1 is in the biogenetically acceptable α-configuration. This configuration leads to the compound D molecule being slightly concave and brings the C-13 methyl group into the shielding line of the C-7 carbonyl group, thus accounting for its unusually high chemical shift. The model also indicates that the 9,11-double bond is very hindered from both sides. On hydrogenation of compound D for 2 h only the furan ring was reduced, leading to the tetrahydrofuran (22).

Structure (20) is a β-vinyloxy-ketone, yet surprisingly this grouping remained unchanged on treatment with methanolic potassium hydroxide, sodium methoxide in boiling toluene, or sulphuric acid under anhydrous conditions even though the isomeric ketone, 11-oxocedrelone (4),[3] is a stable compound. The stability to base may be due to the rigidity of the systems preventing the O–C(1) bond becoming antiperiplanar with a C(2)–H bond. The first product of proton addition to the double bond in the case of unrearranged compound D would be the oxonium ion (30), and models indicate that the products of nucleophilic addition to C-11 with either the 9α(H)- or 9β(H)-isomer of (30) would involve very serious steric interaction between the addendum and the rest of the molecule. It could be therefore that if the ion (30) is formed it loses a proton and reverts to (20) in preference to picking up a nucleophile.

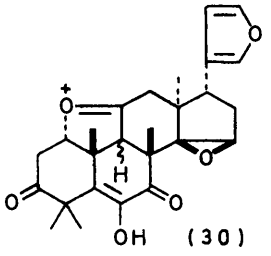
Lack of material has prevented further chemical work on compound D but its ^{13}C n.m.r. spectrum has been determined and is consistent with the proposed structure. ^{13}C Chemical shifts for a number of limonoids have been

[10] R. Hodges, S. G. McGeachin, and R. A. Raphael, *J. Chem. Soc.*, 1963, 2575.

[11] T. Cairns, G. Eglinton, and S. G. McGeachin, *J. Chem. Soc.*, 1965, 1235.

[12] J. W. Powell, *J. Chem. Soc.* (*C*), 1966, 1794.

reported by Taylor [13] and these have been of value in assigning the resonances in the spectrum of compound D (20) and also of anthothecol (1), cedrelone (3), cedrelone acetate (5), and dihydroanthothecol (6) which were determined for comparison and help in assign-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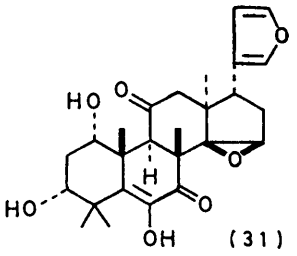
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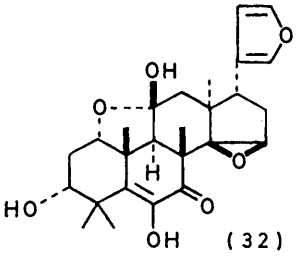
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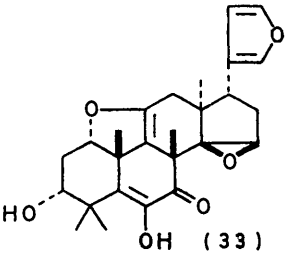
(33)

ments. The spectra were obtained by using broad band decoupling and also narrow off-resonance decoupling. The chemical shifts and multiplicities and probable assignments are listed in Table 2. For values greater than *ca.* 50 p.p.m. the assignments are reasonably certain except possibly those for C-5 and C-6 might require interchanging—there are not many ^{13}C n.m.r. data for diosphenol systems available. For lower values there is less certainty of assignment although there is fairly good agreement between the observed values and those predicted by using simple additivity rules. In all five compounds C-14 and C-15 signals appear at roughly 69 and 56 p.p.m., respectively. The spectrum of compound D clearly shows two carbonyl and eight olefinic sp^2 carbon atoms (including the furan carbons). The doublet at 87.3 p.p.m. fits in well for C-1 in the dihydrofuran ring and the singlet at 110.3 p.p.m. assigned to C-9 shows a chemical shift in good agreement for that of the β-carbon of an enol ether.

The biogenesis of compound D is of interest; one possibility is a pathway from an intermediate such as (31) with a havanesin type of substitution *via* (32) and (33) to compound D (20). Because of steric crowding structure (32) might well easily lose water to give the 9,11-double bond. This would be consistent with the stability of compound D to acid. This pathway involves oxidation at C-11 to a carbonyl group and formation of the acetal (32) before oxidation of the hydroxy-group at C-3. If oxidation to the ketone group at C-3 and elimination of the hydroxy-group from C-1 occurred before ketone formation at C-11 then compound D could only be formed by initial hydration of the C-11 carbonyl group. The resulting geminal diol grouping at C-11 would give rise to considerable steric crowding and hence is unlikely to be formed. This is consistent with the stability of 11-oxocedrelone (4).

TABLE 2

^{13}C N.m.r. spectra (solvent $CDCl_3$; δ_C values; Me_4Si standard)

Carbon atom	Cedrelone (3)	Cedrelone acetate (5)	Anthothecol (1)	1,2-Dihydro-anthothecol (6)	Compound D (20)
C-1	152.4d	151.9d	154.5d	{32.9t}	87.3d
C-2	127.4d	127.6d	126.6d	{36.6t}	32.5t
C-3	203.6s	202.0s	203.4s	205.0s	206.0s
C-4	48.6s	48.8s	49.0s	49s	48.9s
C-5 *	141.3s	141.2s	140.8s	139.7s	142.9s
C-6 *	133.9s	149.6s	133.3s	139.7s	140.1s
C-7	198.0s	194.0s	196.6s	197.0s	196.1s
C-8	46.9s	48.4s	46.3s	47.6s	45.8s
C-9	26.8d	27.7d	27.2d	41.5d (?)	110.3s
C-10/13	40.3s	41.6s	40.6s	39.6s	44.5s
C-11	35.2t	35.2t	69.7d	70.1d	153.4s
C-12	42.1t	42.0t	43.3t	43.2t	42.1t
C-13/10	41.8s	41.9s	41.6s	41.5s	44.8s
C-14	69.8s	69.6s	68.8s	68.9s	70.3s
C-15	55.1d	55.2d	55.9d	56.0d	56.8d
C-16	32.0t	32.0t	31.7t	31.8t	31.5t
C-17	43.2d	43.0d	45.2d	48.4d	38.6d
C-20	123.3s	123.3s	122.8s	122.9s	122.8s
C-21/23	143.1d	143.0d	143.2d	143.0d	143.2d
C-22	110.7d	110.7d	110.7d	110.6d	110.8d
C-23/21	139.5d	139.5d	139.5d	139.5d	139.6d
CCH_3	23.9	23.9	24.2	24.7	29.2
	23.1	23.1	22.8	22.7	25.5
	21.3	22.6	21.9	21.7	21.1
	20.2	20.7	21.4	21.4	20.6
	19.5	19.7	21.1	20.5	17.6
CH_3CO		168.7	169.4	169.3	
CH_3CO		19.0	19.7	15.3	

* These rows may require to be interchanged.

[13] D. A. H. Taylor, *J.C.S. Perkin I*, 1974, 437.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. Optical rotations were determined for solutions in chloroform on a Perkin-Elmer 141 automatic polarimeter. U.v. spectra were recorded for solutions in ethanol. I.r. spectra were determined for solutions in chloroform unless otherwise stated. ^{1}H N.m.r. spectra were determined at 60, 90, or 100 MHz and ^{13}C n.m.r. spectra were recorded on a Bruker WH90 instrument for solutions in deuteriochloroform with tetramethylsilane as internal standard.

For t.l.c., unbaked Kieselgel $HF_{254+366}$ plates were used. For p.l.c. Kieselgel $PF_{254+366}$ plates were used in two sizes (100 cm × 20 cm × 1 mm and 20 cm × 20 cm × 1 mm), referred to as 'large' and 'small' respectively. Light petroleum refers to the fraction with b.p. 40—60°.

Extraction of Khaya anthotheca.—Planks of commercial mahogany timber (*K. anthotheca*) were reduced to shavings and the shavings milled through a 0.125 in sieve. The powdered wood (4.7 kg) was extracted with redistilled light petroleum (4 × 18.5 l) by soaking the wood in the cold and decanting the solvent. The total extraction time for four cycles was 17 weeks. Removal of solvent gave the total crude extract (22.36 g, 0.48%) as an orange gum. Crystallisation twice from ether–methanol gave a sterol (0.5 g, 0.01%), the t.l.c. behaviour and i.r. spectrum of which indicated that it was β-sitosterol. The crude extract was adsorbed from benzene (70 ml) on alumina (type H; 10% deactivated with aqueous 10% acetic acid; 1.9 kg). The column was eluted with ether–light petroleum mixtures from 0 to 100%.

Ether–light petroleum (1 : 19) gave a gum (0.927 g) which was chromatographed on two large p.l.c. plates [two elutions with ether–benzene (1 : 9)]. Two products were obtained. The less polar product (108 mg) was crude azadirone (see below) which was purified by p.l.c. on two small plates, with ether–hexane (1 : 5) as eluant, and combined with material obtained later. The more polar product (420 mg) when dissolved in methanol formed a gel. After a week 24-methylenecycloartanol crystallised as plates (196 mg, 0.004%), m.p. 121—122.5°, $[\alpha]_D^{20}$ +48° (*c* 0.9), M^+ 440 (Found: C, 84.2; H, 12.0. Calc. for $C_{31}H_{52}O$: C, 84.5; H, 11.9%), $\nu_{max.}$ (CCl_4) 3 620, 1 640, 1 096, 1 047, 1 036, 1 023, and 890 cm^{-1}, τ 5.32 (2 H, m, methylene), 6.7 (1 H, m, C-3), 8.94, 9.01, 9.03 (×2), 9.09 (×2), and 9.18 (7 methyls), and 9.42, 9.46, 9.65, and 9.69 (2 H, ABq, C-19) (lit.,[14] m.p. 122°, $[\alpha]_D$ +43°). Further elution with ether–light petroleum (1 : 19) gave a gum (1.10 g) which was chromatographed on three large p.l.c. plates [elution with ether–petroleum (1 : 9)]. The main band (400 mg) afforded rods from ether–methanol. Recrystallisation a second time gave compound A as plates, m.p. 159—160°, $[\alpha]_D^{20}$ +12° (*c* 0.4) (Found: M^+, 428.4013. Calc. for $C_{30}H_{52}O$: *M*, 428.4018), $\nu_{max.}$ 3 590, 3 400br, 1 220br, 1 045, and 1 020 cm^{-1}, τ 4.81br (1 H, d, *J* 6 Hz), 5.32br (1 H, d, *J* 5 Hz), 6.8 (1 H, m), and 8.9—9.5 (complex methyl region). The mother liquors of this compound afforded more azadirone (total 420 mg, 0.009%) which did not crystallise, M^+ 436, $\nu_{max.}$ 1 715, 1 667, 1 255, 1 220br,sh, 1 030, and 880 cm^{-1}, τ 2.82 and 2.94 (2 H, complex, furan α-H), 3.03 (1 H, d, *J* 10 Hz, C-1), 3.89 (1 H, m, furan β-H), 4.33 (1 H, d, *J* 10 Hz, C-2), 4.78 and 4.88 (2 H, m, C-7, C-15), 8.05 (3 H, s, Ac), and 8.77, 8.80, 8.92 (×2), and 9.20 (5 methyls). The n.m.r. spectrum was identical with the spectrum of azadirone.[6]

Ether–light petroleum (3 : 37) eluted more β-sitosterol. This was identified by t.l.c. but not purified further. Elution with ether–light petroleum (1 : 9) gave a mixture (0.652 g) which, after several p.l.c. separations in ether–benzene, afforded two compounds:

(a) *Compound D* (1α,11:14β,15β-*diepoxy*-6-*hydroxymeliaca*-5,9,20,22-*tetraene*-3,7-*dione*) (20) (172 mg, *ca.* 0.004%) crystallised from benzene–hexane as needles, m.p. 242° (decomp.), $[\alpha]_D^{20}$ −7° (*c* 0.8), M^+ 436 (Found: C, 71.35; H, 6.6. $C_{26}H_{28}O_6$ requires C, 71.5; H, 6.5%), $\nu_{max.}$ 3 415, 3 000s, 2 977, 2 934, 2 872, 1 723, 1 690, 1 668, 1 624, 1 112, 933, 879, and 848 cm^{-1}, τ 2.63 (1 H, m, furan α-H), 2.84 (1 H, m, furan α-H), 3.46 (1 H, s, OH), 3.84 (1 H, m, furan β-H), 5.47 (1 H, t, *J* 8.5 Hz), 6.05br (1 H, s), 7.08 (2 H, d, *J* 8.5 Hz), 7.1—8.2 (5 H, complex, and 8.42, 8.56, 8.62, 8.79, and 9.57 (5 methyls), $\lambda_{max.}$ 276 nm (ε 9 980) shifting to 331 nm (ε 5 890) on addition of ethanolic sodium hydroxide.

(b) *Compound B* (7α,11β-*diacetoxymeliaca*-1,14,20,22-*tetraen*-3-*one*) (10) (186 mg, *ca.* 0.004%) crystallised from benzene–hexane as prisms, m.p. 230—231° (decomp.), $[\alpha]_D^{20}$ +31° (*c* 1.0), M^+ 494 (Found: C, 73.3; H, 7.7. $C_{30}H_{38}O_6$ requires C, 72.85; H, 7.7%), $\nu_{max.}$ 1 730, 1 670, 1 500, 1 248, 1 225br,sh, 1 030, 988, and 879 cm^{-1}, τ 2.67 (1 H, m, furan α-H), 2.79 (1 H, m, furan α-H), 2.89 (1 H, d, *J* 10 Hz, C-1), 3.76 (1 H, m, furan β-H), 4.14 (1 H, d, *J* 10 Hz, C-2), 4.25 (1 H, m, C-11), 4.53 and 4.80 (2 H, m, C-7, C-15), 7.89 and 8.06 (2 Ac), and 8.50, 8.55, 8.92 (×2), and 9.23 (5 methyls), $\lambda_{max.}$ 217 nm (ε 16 500).

Elution with ether–petroleum (1 : 4) afforded a gum (0.870 g) which was chromatographed on three large p.l.c. plates [two elutions with ether–benzene (1 : 9)]. Four products were obtained, two of which corresponded to compounds B and D. One, obtained in very low yield, was not studied further but the fourth, *compound C* (7α,11α-*diacetoxymeliaca*-1,14,20,22-*tetraen*-3-*one*) (11) (130 mg 0.003%), was obtained crystalline after two purifications by p.l.c. on small plates. Recrystallisation from methanol gave plates, m.p. 153.5—154.5°, $[\alpha]_D^{20}$ −7° (*c* 0.75), M^+ 494, $\nu_{max.}$ 1 730, 1 670, 1 500, 1 247, 1 220br,sh, 1 029, 986, and 879 cm^{-1}, τ 2.81 (1 H, m, furan α-H), 2.92 (1 H, m, furan α-H), 3.10 (1 H, d, *J* 11 Hz, C-1), 3.91br (1 H, s, furan β-H), 4.39 (1 H, d, *J* 11 Hz, C-2), 4.66 (1 H, m, C-11), 4.74 and 4.86 (2 H, m, C-7, C-15), 7.96 and 8.02 (2 Ac), and 8.71, 8.73, 8.91, 8.93, and 9.14 (5 methyls).

Further elution with ether–petroleum gave a semi-crystalline mass (2.426 g). Recrystallisation from benzene–hexane and then from acetone–hexane afforded anthothecol (723 mg, 0.015%) as a granular solid, m.p. 225—228°, $[\alpha]_D^{20}$ −67° (*c* 0.9), M^+ 480, i.r. and n.m.r. spectra identical with the spectra of an authentic sample, $\lambda_{max.}$ 281 nm (ε 10 500), shifting to 326 nm (ε 5 640) on addition of ethanolic sodium hydroxide (lit.,[2] m.p. 225°, $[\alpha]_D$ −63°). More anthothecol was obtained from the mother liquors. T.l.c. showed the presence of compound D in the mother liquors.

Hydrolysis of Compound B (10).—Compound B (123 mg) was left at 20 °C for 40 h in methanolic potassium hydroxide (5%; 5 ml) containing ethanol (2 ml). Work-up gave a mixture whose n.m.r. spectrum showed a singlet at τ 8.06. The mixture was then heated under reflux for 2.7 h with methanolic potassium hydroxide (5%; 5 ml). Work-up gave a product which yielded 7α,11β-*dihydroxymeliaca*-1,14,20,22-*tetraen*-3-*one* (13) as prisms on recrystallisation

[14] G. Ohta and M. Shimizu, *Chem. and Pharm. Bull.* (*Japan*), 1958, **6**, 325.

from acetone–hexane; m.p. 224—225° (decomp.), $[\alpha]_D^{20}$ +8° (*c* 0.8), M^+ 410, $\nu_{max.}$ 3 600, 3 540, 3 460br,sh, 1 665, 1 500, 1 230br, 1 160, 1 043, 1 030, 960, 912, and 879 cm^{-1}, τ (90 MHz) 2.54 (1 H, d, *J* 11 Hz, C-1), 2.63 (1 H, m, furan α-H), 2.74 (1 H, m, furan α-H), 3.72 (1 H, m, furan β-H), 4.13 (1 H, d, *J* 11 Hz, C-2), 4.36 (1 H, m, C-15), 5.26 (1 H, m, C-11), 6.05 (1 H, m, C-7), and 8.42, 8.56, 8.83, 8.90, and 9.25 (5 methyls).

Oxidation of the Diol (13) *from Compound B*.—The diol (62 mg) was dissolved in dichloromethane (1 ml) and added to a solution (6 ml) prepared by adding chromium trioxide (1.2 g) to a stirred solution of pyridine (2 ml) in dichloromethane (30 ml) at 20 °C and keeping the mixture for 30 min before use. After 30 min the solution was diluted with ether, washed with aqueous sodium hydroxide (5%; 3 × 8 ml) and dilute hydrochloric acid (8 ml), and then dried. Removal of the solvent gave the crude hydroxydiketone (14) (52 mg) as a gum (see later for details of a crystalline sample), τ 2.73 (1 H, d, *J* 10 Hz, C-1), 2.78 (1 H, m, furan α-H), 2.91 (1 H, m, furan α-H), 3.92 (1 H, m, furan β-H), 4.36 (1 H, d, *J* 10 Hz, C-2), 4.41 (1 H, m, C-15), 5.94 (1 H, m, C-7), and 8.59, 8.78, 8.88, 8.90, and 9.03 (5 methyls). The crude material was left for 25 h at room temperature in the oxidising solution (2 ml) described above. Work-up gave the triketone (15) as a gum (see later for details of a crystalline sample), $\nu_{max.}$ 1 710, 1 670, and 878 cm^{-1}, τ 2.77 (1 H, d, *J* 10 Hz, C-1), 2.78 (1 H, m, furan α-H), 2.91 (1 H, m, furan α-H), 3.92 (2 H, m, C-15, furan β-H), 4.27 (1 H, d, *J* 10 Hz, C-2), and 8.36, 8.57, 8.84, 8.87, and 9.05 (5 methyls).

Hydrolysis of Compound C (11).—Compound C (50 mg) was heated under reflux for 4 h with methanolic potassium hydroxide (5%; 5 ml) and then left overnight at 20 °C. Work-up by extraction with ethyl acetate was used owing to the insolubility of the product in ether. The crude product (28 mg) crystallised from chloroform–acetone to give 7α,11α-*dihydroxymeliaca*-1,14,20,22-*tetraen*-3-*one* (16) as needles, m.p. 279—280° (decomp.), M^+ 410, virtually insoluble in chloroform.

Oxidation of the Diol (16) *from Compound C*.—A solution of the diol in pyridine (4 ml) was added to a slurry of chromium trioxide (100 mg) in pyridine (1.5 ml). The mixture was left overnight at 20 °C and then poured into water (100 ml). This was extracted with ether (3 × 40 ml) and the combined extracts were washed with dilute hydrochloric acid and dried. Removal of the solvent gave a gum (18 mg) which was chromatographed on a large t.l.c. plate [elution once with ether–hexane (1 : 1)]. Two products were obtained. The more polar product (4 mg) was 7α-*hydroxymeliaca*-1,14,20,22-*tetraene*-3,11-*dione* (14), which crystallised from ether as prisms, m.p. 222—224°, M^+ 408, $\nu_{max.}$ 3 540, 3 400br, 1 700, 1 665, 1 230br, 1 108, and 878 cm^{-1}, n.m.r. spectrum identical with that of the hydroxydiketone obtained from compound B.

The less polar product (5 mg) was *meliaca*-1,14,20,22-*tetraene*-3,7,11-*trione* (15), which crystallised from acetone–hexane as prisms, m.p. 202—204°, M^+ 406, $\nu_{max.}$ 1 710, 1 670, 1 500, 1 289, 1 181, 1 172, 1 108, 1 033, and 878 cm^{-1}, identical with the triketone from compound C (t.l.c. and n.m.r. spectrum).

Methylation of Compound D (20).—Sodium (7 mg) was added to a solution of compound D (42 mg) in sodium-dried toluene (1 ml) containing several drops of methanol. The mixture was heated under reflux for 1.6 h and methyl iodide (an excess) was added. The mixture was heated under reflux for a further 1.2 h and cooled. Water (25 ml) was added and the mixture was extracted with ether (3 × 15 ml). The combined extracts were washed with dilute hydrochloric acid and dried. Removal of solvent gave the crude methyl ether (48 mg) as a gum. This was purified by p.l.c. on one small plate [elution twice with ether–hexane (1 : 1)]. The pure product, 1α,11:14β,15β-*diepoxy*-6-*methoxymeliaca*-5,9,20,22-*tetraene*-3,7-*dione* (21), was obtained as a gum, M^+ 450, $\nu_{max.}$ 1 725, 1 693, 1 689sh, 1 679, 1 589, 1 500, 1 256, 1 220br, 1 177, 1 120, 1 051, 1 019, 932, 913, and 879 cm^{-1}, τ 2.63 (1 H, m, furan α-H), 2.84 (1H, m, furan α-H), 3.82 (1 H, m, furan β-H), 5.54 (1 H, t, *J* 8.5 Hz), 6.06br (1 H, s), 6.87 (3 H, s, OMe), 7.09 (2 H, d, *J* 8.5 Hz), and 8.47, 8.58, 8.63, 8.82, and 9.48 (5 methyls), $\lambda_{max.}$ 258 nm (ε 9 000).

Treatment of Compound D (20) *with Methanolic Potassium Hydroxide*.—Compound D (21 mg) was heated under reflux with methanolic potassium hydroxide (5%; 10 ml) for 6.5 h and the solution was then poured into dilute hydrochloric acid (50 ml). This was extracted with ether (3 × 15 ml) and the extract was dried and evaporated to give an orange solid (20 mg) which showed mainly starting material on t.l.c. The n.m.r. spectrum of the solid was identical with that of starting material.

Hydrogenation of Compound D (20).—Compound D (33 mg) in reagent grade ethyl acetate (10 ml) containing palladium–charcoal (10%; 14 mg) was hydrogenated at atmospheric pressure for 3.6 h. The solution was filtered and the solvent removed to give the tetrahydro-product (22) as a gum (33 mg), which gave no colour on t.l.c. with Ehrlich's reagent; M^+ 440, $\nu_{max.}$ 3 400, 1 720, 1 690, 1 665, 1 620, 1 260, 1 235br,sh, and 1 039 cm^{-1}, τ 3.45 (1 H, s, OH), 5.52 (1 H, t, *J* 8.5 Hz), 6.19br (1 H, s), 6.05—6.45 (3 H, complex, tetrahydrofuran α-H), 6.85 (1 H, m), 7.04 (2 H, d, *J* 8.5 Hz), 8.38, 8.57, 8.62, and 8.83 (4 methyls), and 9.33 and 9.36 (3 H, Me of two C-20 epimers), $\lambda_{max.}$ 227 nm shifting to 326 nm on addition of ethanolic sodium hydroxide.

Treatment of Compound D (20) *with Sulphuric Acid*.—Compound D (30 mg) was dissolved in ether (60 ml) and concentrated sulphuric acid (0.6 ml) was added. The ether was slowly boiled off leaving a purple residue. Water (50 ml) was cautiously added and the resulting mixture extracted with ether (3 × 20 ml). The combined extracts were dried and evaporated to give a yellow gum which was applied to a small p.l.c. plate. One elution with ether–hexane (1 : 1) afforded the main product (25) (12 mg) as a gum which did not crystallise, M^+ 436, $\nu_{max.}$ 3 400, 1 720, 1 649, 1 610, 1 500, 1 260, 1 164, 1 112, 1 062, 1 040, 987, 921, 878, and 870s cm^{-1}, τ 2.74 (1 H, m, furan α-H), 2.92 (1 H, m, furan α-H), 3.56 (1 H, s, OH), 3.68 (1 H, m, furan β-H), 4.59br (1 H, s, OH), 5.54 (2 H, complex), 7.05—7.25 (6 H, complex), and 8.35, 8.41, 8.57, 8.61, and 8.92 (5 methyls), $\lambda_{max.}$ 233 (ε 10 100) and 291 (7 900) shifting to 233 (11 250) and 362 nm (ε 3 700) on addition of ethanolic sodium hydroxide.

Treatment of Anthothecol (1) *with Sulphuric Acid*.—Anthothecol (207 mg) was dissolved in ether (50 ml) and concentrated sulphuric acid (1 ml) was added. The ether was slowly boiled off leaving a brown residue. Water (50 ml) was cautiously added and the resultant solution extracted with ether (3 × 20 ml). The combined extracts were dried and evaporated to give the crude product (163 mg). This was chromatographed on two small p.l.c. plates [elution once with ether–hexane (1 : 1)]. The main

product (90 mg) gave isoanthothecol (27) as needles (from acetone–hexane), m.p. 175° (decomp.) with drastic softening around 105°, $[\alpha]_D^{20}$ −45° (*c* 0.8), M^+ 480 (Found: C, 69.4; H, 6.9. Calc. for $C_{28}H_{32}O_7$: C, 70.0; H, 6.7%), $\nu_{max.}$ 3 420, 1 740br, 1 705br, 1 689sh, 1 665, 1 628, 1 500, 1 296, 1 225br, 1 098, 1 064, 1 030, 980, 916, and 879 cm^{-1}, τ 2.55 (1 H, m, furan α-H), 2.61 (1 H, d, *J* 10 Hz, C-1), 2.66 (1 H, m, furan α-H), 3.47 (1 H, m, furan β-H), 4.01 (1 H, d, *J* 10 Hz, C-2), 4.86 (1 H, m, C-11), 5.26br (1 H, s, OH), 5.44 (1 H, q, *J* 7 and 8 Hz, C-15), 7.89 (3 H, s, $MeCO_2$), and 8.44 (×2), 8.47, 8.68, and 8.72 (5 methyls), $\lambda_{max.}$ 233 (ε 18 400) and 287 (10 860) shifting to 233 (19 860) and 358 nm (6 024) on addition of ethanolic sodium hydroxide (lit.[3] for isoanthothecol, m.p. 125°).

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